

How Exercise, Fewer Calories, Plant Toxins May Protect Our Brains

BY DANA TALESNIK

Outside of the lab, neuroscientist Dr. Mark Mattson loves to go running. In fact, NIH's may have seen him and his Baltimore-based lab mates compete in the annual NIH Institute Relay on campus, where they have placed in the top 3 of about 100 teams for the past 3 years.

In the lab, Mattson and his colleagues are racing to uncover the potential of exercise, fasting and consuming certain plant chemicals to improve brain function and thwart neurodegenerative disease.

"These energetic challenges—[fasting

and exercise]—enhance synaptic plasticity, protect neurons during aging and maybe protect against neurodegenerative disorders," said Mattson, chief of NIA's Laboratory of Neurosciences. He spoke at a Jan. 6 seminar titled, "What Doesn't Kill You...Why Some Plant 'Toxins' May Bolster Brain Health."

Exercise, Fasting May Improve Brain Function

As modern medicine helps more people live longer, more men and women are in danger of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases, for which there's still no effective treatment. But do lifestyle habits affect brain health? They very well might.

As we age, brain cells endure oxidative damage and local inflammation that can compromise synapse function and cause

SEE **MATTSON**, PAGE 8



Intermittent fasting is beneficial to man and beast, Dr. Mark Mattson has found.



'Snowzilla' hits NIH. See story on back page.

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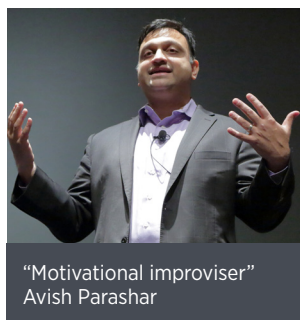
SINCE WORKLIFE IS UNSCRIPTED Planning to Handle the Unplanned Like a Pro

BY CARLA GARNETT

How good are you at handling a sudden change in plans? What if your success at work depended on it? At a recent Deputy Director for Management Seminar, the self-described

"world's only motivational improviser" Avish Parashar offered a few suggestions.

"Life isn't scripted—no matter how much we want it to be, with our agendas and our to-do lists and our productivity apps and our big-picture vision boards," he said, holding up



"Motivational improviser" Avish Parashar

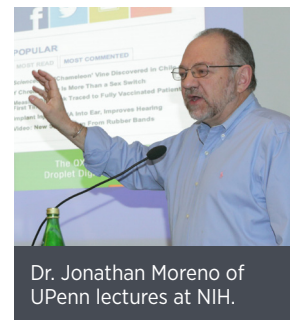
SEE **PARASHAR**, PAGE 6

'Military' Uses of Neuroscience Have Tended to Stumble, Moreno Says

BY RICH MCMANUS

At the height of the Cold War more than half a century ago, LSD research failed the acid test when investigators, hoping the drug would render its takers unable to lie, found instead that users were unable to be coherent.

In the intervening decades, many attempts by U.S. military and security interests to harvest discoveries in neurobiology and psychology for their own uses have fallen as flat as an unwittingly dosed soldier, staggering stoned in a meadow.



Dr. Jonathan Moreno of UPenn lectures at NIH.

SEE **MORENO**, PAGE 4



NIH Hosts Rare Disease Day, Feb. 29

On Monday, Feb. 29, NIH will host Rare Disease Day, which takes place from 8:30 a.m. to 3:30 p.m. in Masur Auditorium, Bldg. 10. Speakers include Rep. Leonard Lance (R-NJ); NIH director Dr. Francis Collins; NCATS director Dr. Christopher Austin; Clinical Center director Dr. John Gallin; and NCATS Office of Rare Diseases Research and Division of Clinical Innovation director Dr. Petra Kaufmann.

The event will feature presentations, posters and exhibits, tours of the Clinical Center and an art show. Admission is free and open to the public. In association with Global Genes, participants are encouraged to wear their favorite pair of jeans.

Prior to the event, on Feb. 22, NIH will host a Twitter chat on rare diseases from 2 to 3 p.m. with Collins and Austin. Join the conversation by following #NIHChat.

To see the Rare Disease Day agenda and to register, visit https://events-support.com/events/NIH_Rare_Disease_Day. Follow the event on social media at #RDDNIH.

Symposium Honors Female FARE Winners

Feb. 29

Each year, the NIH women scientist advisory committee selects two or three female winners of the Fellows Award for Research Excellence (FARE) to be honored as WSA Scholars for their outstanding scientific research. To honor the WSA FARE winners, a symposium will be held on Monday, Feb. 29 at 2:30 p.m. in Wilson Hall, Bldg. 1. Each scholar will present her work and the talks will be followed by a reception. All are invited to attend.

The 2016 WSA FARE winners and their topics are:

Dr. Sigal Shachar, "Systematic identification of genome positioning factors by high-throughput screening"

Dr. Heekyoung Bae, "Deletion of the IFN-gamma 3' UTR AU-rich element results in primary biliary cirrhosis in female C57/BL6 mice"

Dr. Neelam Debas Sen, "Tale of two DEAD-box RNA helicases: Ded1 and eIF4A have distinct but overlapping functions in regulating eukaryotic translation initiation in vivo."



Bowles To Give NINR Director's Lecture, Mar. 3

Dr. Kathryn H. Bowles will present the first 2016 NINR Director's Lecture on Thursday, Mar. 3 from 1 to 2 p.m. in Lipsett Amphitheater, Bldg. 10. Her talk "Innovations to Improve Discharge Planning" will describe her studies using information technology to improve care for older adults.

Her journey began with a clinical question and includes co-founding a software company, which was awarded two Small Business Innovation Research grants from NINR, to further develop and distribute her team's work aimed at improving discharge planning and decision-making following release from the hospital.

Bowles is the van Ameringen professor in nursing excellence, director of the Center for Integrative Science in Aging at the University of Pennsylvania School of Nursing and vice president and director of the Center for Home Care Policy and Research at the Visiting Nurse Service of New York. Her ongoing study, funded by NINR, focuses on the development of decision-support tools to determine the best site of care for those needing care following hospital discharge. Bowles's other research interests include telehealth technology, home care and evaluation of electronic health records.

The NINR Director's Lecture Series is designed to bring the nation's top nurse scientists to campus to share their work and interests with a trans-disciplinary audience. The event is free and open to the public. For more information and to register, visit www.ninr.nih.gov/directorslecture.



NIH To Celebrate Pi Day, Mar. 14

NIH will hold a Pi Day Celebration on 3.14 (Mar. 14). Pi Day is observed on this day around the world; to see how others are marking it, visit www.piday.org. The goal of the NIH event is to increase awareness across the community of the role that the quantitative sciences play in biomedical science.

The day will be packed with events, including a keynote address by Dr. Carlos Bustamante, chair of Stanford's new department of biomedical data science (1 p.m., Lipsett Amphitheater, Bldg. 10). The lecture will be open to the public and available by videocast.

Other events include:

- PiCo Lightning Talks — 3 slides, 1 idea, 4 minutes (10-11 a.m.)
- Poster/Demo Session and Networking Event, with food provided by FAES (11 a.m.-1 p.m.)
- Workshop on Reproducible Research, (2:30-4:30 p.m.)
- Pi Day Scholars Event for high school students and their teachers (all day)
- Pies by Eurest available for purchase and donation

Join the Pi Day conversation—include #NIH_PiDay in your tweets. For more information, including a schedule of events, visit <https://datascience.nih.gov/PiDay2016>.

Sailing Association To Hold Open House

Mar. 9

The NIH Sailing Association invites everyone to its open house on Wednesday, Mar. 9 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln.

Explore your interest in learning to sail and discover opportunities for sailing with NIHS. There will be information about 6-week basic training classes, boat chartering, the club's racing program and social activities offered by NIHS. A fee of \$5 at the door includes pizza, drinks and snacks. Cash bar for beer and wine—\$2 each.

Look for NIHS posters and flyers around campus. Registration is now open for the spring (April-May) and summer (July-August) basic training classes.

For more information, visit www.nihsail.org/.

New NIH Toolbox App Captures Reliable Research Data

BY ERIN CALHOUN

Data. It reveals health trends. It uncovers associations between risk factors and disease and helps develop interventions for preventing and treating various conditions. Our reliance on data is at the heart of research. But capturing data can be challenging.

Imagine collecting an entire battery of measurements—a whole world of research e-data—using tried and true metrics. That capability exists and it's literally just a click away.

The NIH Toolbox is a set of brief, psychometrically sound measures for researchers and clinicians assessing motor, emotional, sensory and cognitive function in people ages 3 to 85. It provides 104 well-validated measures, across 52 domains, along with normative data in English and Spanish. What's even better? Individual instruments are typically administered in 1-7 minutes and all 4 batteries can be administered in as little as 2 hours.

"The NIH Toolbox provides a 'common currency' for neurological research," says Dr. Richard Hodes, director of the National Institute on Aging. "Our intent was not only to provide a resource for scientists, but also to encourage its use to enhance comparability across studies. The NIH Toolbox is one important way to help maximize the NIH investment in research on the neurological and behavioral influences on health and longevity."

The toolbox is proving to be a go-to assessment for researchers nationwide. It was rolled out in 2012—by more than 250 contributing scientists from 80 institutions—with funding from the NIH Blueprint for Neuroscience Research and NIH's Office of Behavioral and Social Sciences Research. Over the past few years, the team at Northwestern University, which developed and maintains the toolbox with funding from NIH, has built a robust web site that includes videos and how-to presentations.

"The NIH Toolbox enables economies of scale and enhances efficiency," notes Dr. Richard Gershon, principal investigator



The NIH Toolbox has now upgraded its accessibility by introducing an iPad version available to researchers and clinicians through an app in the iTunes App Store.

PHOTO: NORTHWESTERN UNIVERSITY

and professor and vice chair for research at Northwestern University Feinberg School of Medicine, department of medical social sciences. "It is capable of monitoring neurological and behavioral function over time and measuring key constructs across developmental stages."

Even if you've used the NIH Toolbox in the past, there are some new bells and whistles you'll want to know about.

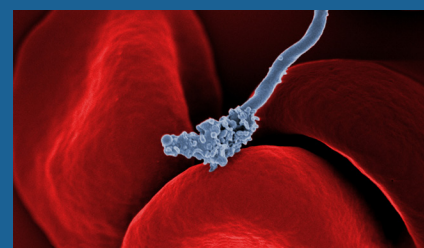
It's gone mobile. Just this summer, the development team at Northwestern introduced an iPad version and measures are now available to researchers and clinicians through an app in the iTunes App Store. You'll need Wi-Fi capacity for initial installation of the app, but you won't need an Internet connection to use it, allowing more ways and places to use the toolbox than before. In order to maintain the integrity of the cognitive measures and ensure they are not accessible for practice or misuse, special permission is required for access to the cognitive battery.

To date, the resource has been used in more than 600 studies. It includes measures that may be of particular interest to researchers and clinicians in the fields of aging and child development. The toolbox has been used among a variety of study populations such as the NIH Human Connectome Project.

"The NIH Toolbox allows researchers to assess function using common metrics and makes it possible to support the pooling and sharing of large data sets," notes Dr. Molly Wagster, NIH lead project officer for development of the NIH Toolbox.

How can it work for you? With the resource, you can measure multiple cognitive domains—including speed of processing, executive function and episodic memory—and generate composite scores. The NIH Toolbox can also be used to assess more than 20 subdomains of emotional function in one minute or less each. Self-report data may be collected on emotional constructs such as self-efficacy, perceived stress, meaning and purpose and emotional support. It allows you to analyze balance data in real time using an iPod in conjunction with the iPad. Other motor battery tests measure dexterity, grip strength, gait speed and endurance. You can also quickly and validly assess audition, visual acuity, vestibular balance, olfaction, taste and pain with the toolbox.

Visit www.nihtoolbox.org to learn more. **R**



ON THE COVER: Electron micrograph of *Borrelia hermsii* bacterium, the causative agent of relapsing fever, interacting with red blood cells.

IMAGE: TOM SCHWAN, ROBERT FISCHER & ANITA MORA, NIAID

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email editor or phone (301) 496-2125.

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The *NIH Record* is recyclable as office white paper.

NIH National Institutes of Health
Turning Discovery Into Health

And as improbable as it sounds, given recent advances in medicine and technology, the old standbys—sex, alcohol and propaganda—remain the cheapest and most effective tools for bending minds.

So reported Dr. Jonathan Moreno, a philosopher and historian at the University of Pennsylvania who spoke at NIH Jan. 11 on a topic that was also the title of his 2006 book: “Mind Wars: Brain Science and the Military in the 21st Century.”

With projects such as the BRAIN Initiative and a European big-data effort known as the Human Brain Project under way, we are now in the “era of Big Neuroscience,” said Moreno. It is a growth industry, now about 15 years old, driven largely by advances in technology.

But for every scientist who sees functional magnetic resonance imaging as a way to advance human health, there is a tactician who wonders if fMRI can be used to scan the thoughts and plans of a potential terrorist.

Moreno reviewed a host of attempts to apply medical knowledge to spycraft, including the use of mescaline as a truth serum, and psychedelics as ego-suppressants and mind-controllers whereby “you could make a discreet man indiscreet.”

History, and YouTube (check out Operation Moneybags or Operation



Moreno recommends ELSI—ethical, legal and social implications—research “before it is too late” for technologies that could be weaponized.

PHOTOS: BILL BRANSON

performance is the goal, Moreno said. One of his colleagues is writing a book whose premise is that all wars in human history have been explicitly drug-dependent, including stimulants and depressants. Recently, there have been widespread reports of ISIS reliance on Captagon, the stimulant cousin of Adderall, to create fearless warriors.

★ ★ ★

“Color me a skeptic about much of [federal investments in blue-sky technologies] ever being deployed. It’s flashy and it’s fascinating, but there’s no budget [compared with conventional weaponry] for it.”

—DR. JONATHAN MORENO

★ ★ ★

Midnight Climax), provide a record of follies undertaken as part of the once-secret MK ULTRA program, which sought to employ LSD as a secret-revealer.

The CIA and the Army lost interest in LSD by the late 1950s, Moreno said, “but commanders have always been concerned about the mind...Every era tries to capitalize on the mind-control technology of the times.”

In addition to the arms race, there is also a “mind race” in which enhanced human

Among the current arsenal of science-based tools, according to Moreno, are: modafinil, a type of amphetamine used by fighters and pilots to sustain concentration; the so-called “trust drug” oxytocin, for use in interrogation; the beta-blocker propranolol, thought to suppress pangs of conscience; a variety of brain-imaging techniques designed either to read minds or impel behaviors; lie detectors that rely on brain waves; and creation of armed robotic warriors that use

sophisticated face-recognition algorithms to identify enemies.

Moreno is under no illusion about the seriousness of the effort to recruit scientific knowledge to tactical advantage; a 2011 study of military expenditures in the cognitive neurosciences showed \$55 million for the Army, \$34 million for the Navy, \$24 million for the Air Force and more than \$240 million for DARPA, “not to mention the millions of dollars invested in black budgets.”

He recommends ELSI—ethical, legal and social implications—research “before it is too late” for any emerging technologies that could conceivably be weaponized. Moreno also said society should be vigilant when entities such as the Defense Intelligence Agency and Office of Naval Research invest heavily in the neurosciences.

But he also grew up, literally, in a mental hospital; his dad was a psychiatrist who specialized in role-playing therapy. He is intimately acquainted with science’s limitations in controlling human behavior.

“Color me a skeptic about much of [federal investments in blue-sky technologies] ever being deployed. It’s flashy and it’s fascinating, but there’s no budget [compared with conventional weaponry] for it.” **R**

Estes To Deliver NIAID Chanock Lecture

Virologist Dr. Mary K. Estes will deliver the 2016 NIAID Robert M. Chanock Memorial Lecture. Her talk, "Understanding Human Noroviruses: A Bench to Bedside Story," will take place on Tuesday, Feb. 23 at 9 a.m. in the Bldg. 50 1st floor conference



Dr. Mary K. Estes

room. The lecture honors Chanock, who served as chief of the NIAID Laboratory of Infectious Diseases for more than three decades.

Estes is the Cullen endowed chair of human and molecular virology and a professor in the department of molecular virology and microbiology at Baylor College of Medicine. In her lecture, she will address her research

to better understand human noroviruses (HuNoVs), the leading causes of gastroenteritis worldwide.

First discovered at NIH by Dr. Al Kapikian using immune electron microscopy in 1972, these significant human pathogens were not well understood for many years for two major reasons: Little was known about the virus's genes and the virus cannot be grown in cell culture. In 1990, Estes's laboratory cloned the viral genome, sequenced it and developed molecular diagnostics, leading to a new understanding of the virus's genes and the significance of these viruses as human pathogens worldwide.

Still, however, HuNoVs do not grow well in cell cultures. Recently, Estes's lab has evaluated whether HuNoVs replicate in new cell culture models called human intestinal enteroids, which would help to understand host physiology as well as host-microbe interactions and pathogenesis. In her presentation, she will discuss the results of these studies and how they have led to a new understanding of HuNoV biology and pathogenesis.

Estes has served on local, state, national and global committees devoted to research and vaccine development. She was co-chair of the board of scientific counselors for NIAID and a scientific advisor for several digestive diseases centers and regional centers of excellence of emerging infections and biodefense. She is a fellow of the American Academy of Microbiology and the American Association for the Advancement of Science and a member of the National Academy of Medicine (formerly the Institute of Medicine), the National Academy of Science and the Academy of Medicine, Engineering and Science of Texas.

LIFESAVERS

NINDS Investigator, Friends Honored for Rescue at Sea

Dr. Eric Wassermann, a staff clinician and chief of the behavioral neurology unit at NINDS, and his crewmates have recently been given a Lifesaving Award by the Humane Society of the Commonwealth of Massachusetts.

Wassermann was on Sparky, a friend's 42-foot Hinckley sailboat, returning from the 2015 Marion, Mass., to Bermuda yacht race when the crew of 4 men and 1 woman overheard a distress call from Restive, another returning boat nearby.

Restive's rudder had come loose, leaving it impossible to steer. More seriously, the loose rudderpost was breaking a hole in the hull and the boat was starting to take on water. Sparky's skipper immediately changed course to intercept the damaged vessel. When Sparky reached the scene in 10- to 15-foot waves and winds gusting over 30 knots, Restive's worried crew had exhausted their options for emergency steering and damage control and had decided to abandon ship.

The boats could not be brought near each other without the risk of serious damage and, 125 nautical miles from shore, they were out of air rescue range. The only choice

seemed to be for Restive's captain and crew of 4 to board their life raft and drift downwind to Sparky.

The decision to leave a floating boat for a life raft is never taken lightly, but deteriorating conditions, the approach of night and the unavailability of other help made the move imperative.

"The scariest part was the thought of losing someone in the transfer," said Wassermann. "In



Dr. Eric Wassermann (l), suffering from seasickness and fatigue, and a crewmate during a "bumpy" part of the race

all our 250 combined years of sailing, none of us had even considered how to recover people from an inflatable raft at sea. If someone went into the water in those conditions, there was no certainty we would get them back."

As it happened, the transfer went smoothly, aside from a nasty cut on one Restive crewmember's leg, which later became infected. Restive was found the next day, nearly full of water, by a salvage operation launched from Nantucket.

Last September, Sparky's captain and crew were awarded the Robert N. Bavier Award for Seamanship or Sportsmanship by the Marion-Bermuda race authorities. Recently, however, the rescue came to the attention of the Humane Society of the Commonwealth of Massachusetts, which awarded the captain and crew its Lifesaving Award and are striking a special plaque for Sparky.

Founded in 1785, the society was formed to reduce loss of life in shipwrecks off the coast of New England. It also raised the initial capital to found the Massachusetts General, McLean and Boston Lying-In (now Brigham) hospitals.



Using games and a volunteer from the Masur Auditorium audience, Parashar demonstrates making snap decisions with improvisation.

Parashar

CONTINUED FROM PAGE 1

a concierge-style bell. “Life is the ultimate improvisation. Just when you think you’ve got it all figured out, the universe comes in and goes, ‘DING! Now deal with this.’ Sometimes ‘ding’ happens.”

Learning a few techniques to make better snap decisions can help everyone in every situation, Parashar noted.

“We all have those moments,” he said, “where because we are angry, frustrated, stressed, overworked or just not thinking, where we end up doing or saying something less than optimal that ends up making our lives more complicated than they need to be.”

Work and the goals you set for your organization can benefit from a little positive improvisation as well.

“Our lives are nothing but a series of moments,” Parashar pointed out. “If we make good decisions in those moments, life gets easier and more successful. If we make bad decisions, life becomes more of a struggle.

“Anyone can do well when everything goes according to plan,” he continued. “The real test—and I would say your value to your organization—is how quickly and effectively you respond when things don’t go according to plan...These skills are more valuable now than ever simply because the

...
“You can never make progress looking backwards. The more time we spend wishing things could be like they were before, the less energy we’re putting toward making this new reality even better.”

—AVISH PARASHAR

...
 back, have fun, it’s going to open up your resources quicker.”

A level two response goes beyond merely reacting. “Adapting” requires more assertive action. “Every ding moment has an opportunity within it,” Parashar explained. “Great improvisers learn how to find and take advantage of those opportunities.”

For most of us, the temptation when facing change is to wish for the way things used to be, he said. However, “you can never make progress looking backwards. The more time we spend wishing things could be like they were before, the less energy we’re putting toward making this new reality even better.”

Adaptability works in increments, step by step, Parashar noted. And the steps don’t have to be all that large. “If you can think of your actions as experiments instead of solutions, you will make much faster progress,” he said. “Take small steps. See what happens. Then adjust.”

Finally, Parashar said, comes master-level

world is changing faster than it ever has before...The key is responding. It’s not what happens, it’s how you respond.”

Parashar described three levels of response: improvise, adapt and innovate.

In straight improv—call it beginner’s improv—Parashar said you learn to take on an improviser’s mindset: “Have fun. Be willing to fail. Focus on what you can control and let go of the rest.”

Using games and volunteers from the Masur Auditorium audience, the professional impro-

viser admitted it’s not always easy.

“Ding moments aren’t fun,” he said. “They throw us off course...Failure does have consequences, but fear of failure will do nothing but paralyze you, cut off your creativity when you need it most... Bring a positive energy to it...If in those moments of stress and change you can step



At the lively, humor-filled seminar, attendees react to absurd scenarios Parashar and his helpers inadvertently created. Responding with such levity in real life to sudden or unexpected situations in the workplace is much more difficult, but can offer similar pleasant rewards, according to the speaker.

PHOTOS: ERNIE BRANSON



Parashar advises, "Take small steps. See what happens. Then adjust."

improvisation: Innovation. That's when you don't wait for change to happen to you, but decide yourself to head in another direction. "Create your own ding moments that change the game and propel you forward," he suggested to those who feel they or their program may be stuck in a rut. "Do something new or do something old in a new way."

Parashar even has a sort of script for changing your script. When a colleague or coworker comes to you with what may seem like a cockamamie proposal, the professional improv guy wants you to "say 'yes and' instead of 'yes but.'"

Really, Parashar said, it's more of a mindset, an attitude that changes the energy of the conversation from negative and constrictive to expansive and collaborative.

"This is not a literal technique," he explained. "It's a mentality...We're talking about ding moments and default responses. For so many, the default response to anything unexpected, different, new, out-of-our-comfort-zone, not-how-we-originally-wanted-it-to-be is to immediately say, 'yes but.' All I'm suggesting is that we can reap some tremendous benefits if we switch our default response to 'yes and.'"

Such an approach not only changes the dynamic of the interaction, but also helps the relationship. "[The more positive attitude] heads off conflict, opens up creativity," he said. "[NIH] is a place of creativity. 'Yes and' drives it."

Concluding the lively, humor-filled seminar, Parashar urged attendees to use improvisation boldly for it to be most effective. "You must say 'yes and' even to ideas that seem impossible." After all, anyone can approve a good idea. "Sometimes the best ideas are hiding behind the worst ones." **R**

Craven To Speak in NLM Series, Mar. 9

The next speaker in the National Library of Medicine Informatics Lecture Series will be Dr. Mark Craven, discussing "Inferring Host-Pathogen Interactions from Diverse Data Sources" on Wednesday, Mar. 9 from 2-3 p.m. in Lister Hill Center Auditorium, Bldg. 38A.



Dr. Mark Craven will give the next NLM Informatics Lecture.

Craven is a professor in the department of biostatistics and medical informatics at the University of Wisconsin and an affiliate faculty member in the department of computer sciences. He is director of the Center for Predictive Computational Phenotyping, one of NIH's Centers of Excellence for Big Data Computing. He is also director of the NIH/NLM-funded Computation and Informatics in Biology and Medicine Training Program and a member of the Institute for Clinical and Translational Research, the Carbone Cancer Center and the Genome Center of Wisconsin.

Craven will discuss his work in three studies that involve developing and applying predictive methods in order to characterize host-pathogen interactions.

Sign language interpreters will be provided. Individuals who need reasonable accommodation to participate should contact Ebony Hughes at (301) 451-8038 or Ebony.Hughes@nih.gov or the Federal Relay (1-800-877-8339).

The talk will be broadcast live and archived at <http://videocast.nih.gov/>.

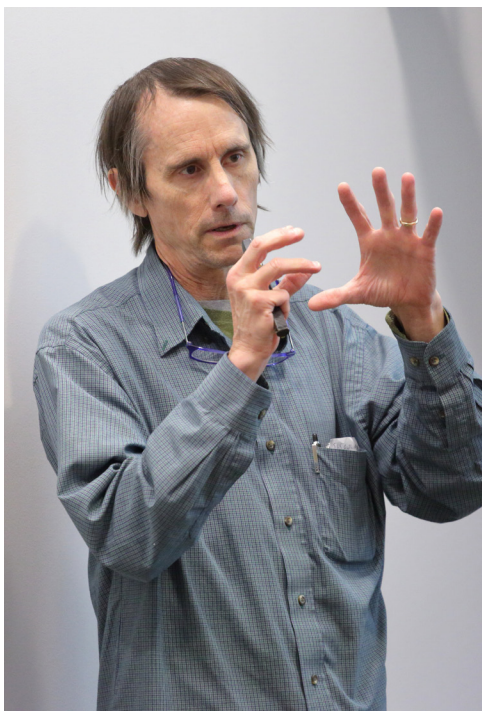
FEEDBACK

Have a question about some aspect of working at NIH? You can post anonymous queries at <https://nihrecord.nih.gov/> (click on the Feedback tab) and we'll try to provide answers.

Feedback: Would it be possible for NIH to allow for 2 car entrance lanes after 10 a.m. in situations where the government has a 2-3 hour weather-related delay? When I entered at Old Georgetown Rd. and Center Dr. today [Jan. 28], there was only 1 lane open at 10:05 a.m. and there was a gigantic back-up of cars waiting to enter NIH from Old Georgetown Rd. (causing a traffic jam). I asked one of the two officers if they could open up the second entrance lane due to the huge traffic back-up, and he said, "No, that is against NIH policy." While that may be true, I think it's time to change that policy on weather-delay days.

Response from the Office of Research Services, NIH Police: Yes. Although the decision is based on the specific situation, and not just for weather-related delays, police officers are authorized to keep an entrance or entrances open and staffed with attendant personnel as long as necessary. However, the decision will be based on actual conditions—if traffic is heavy, the entrance will remain open; if traffic is light, it will close at its designated time.

The NIH Police have limited resources but strive to utilize them prudently and effectively. We will reiterate to our officers that they are empowered to make traffic decisions based on their best judgment and the particular circumstances presented.



Mattson's research has informed his lifestyle, including diet and exercise regimens.

PHOTOS: ERNIE BRANSON

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“From a lifelong health perspective, it’s important to challenge yourselves and your organ systems intermittently with things like exercise, not overeating, maybe even fasting a little bit. Maybe skip breakfast or lunch, then exercise, then eat.”

—DR. MARK MATTSON

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enhance DNA repair. People who exercise throughout their lives, he said, are less likely to develop dementia.

Meanwhile, intermittent fasting studies on animals and people, he said, show improved glucose regulation and lipid profile and activated adaptive stress response pathways in cells. His lab found that mice fasting on alternate days before given a neurotoxin that damages the same neurons affected in Alzheimer’s had less learning and memory deficits. In stroke models, they also found less brain damage. In a Huntington’s disease model, intermittent fasting before the mice were symptomatic also delayed onset of motor dysfunction and protected neurons.

As our brains process information, neurons are active and levels of BDNF (brain-derived neurotrophic factor, a protein that helps protect neurons) increase. Mattson’s lab found that exercise and fasting can increase production of BDNF.

If the hippocampus, the brain region critical for learning and memory, doesn’t function optimally, short-term memory gets lost—a main symptom of Alzheimer’s—and nerve cells degenerate.

“So not only does exercise and intermittent fasting strengthen existing synapses,” said Mattson, “we think it promotes an increased number of neurons and formation of new circuits in the hippocampus.”

Some neurological pathways affected by exercise and fasting are also affected by phytochemicals (plant compounds), which may protect cells against injury and disease, said Mattson.

Everything in Moderation

In contrast to animals, plants cannot run away from potential predators such as insects and the ever present grazing deer. Instead, to protect themselves from such

predators, plants produce natural pesticides, bitter-tasting chemicals that act as a natural deterrent.

“There is emerging evidence that at least some of the chemicals in fruits, vegetables and other plants we eat, from an evolutionary perspective, their function is to dissuade insects and other organisms such as us from eating them,” said Mattson. But, over time, he said, animals and people have adapted to protect themselves from the potential toxic effects of these chemicals.

While some of these phytochemicals could be toxic, even lethal, at high doses, studies show many have health benefits when consumed in smaller amounts—a process called hormesis. Some of these chemicals upregulate our adaptive stress response and inhibit inflammation—which is important in Alzheimer’s and Parkinson’s research, said Mattson. Other phytochemicals can modulate pathways involved in energy metabolism and neurotrophic signaling.

Mattson’s lab recently tested 50 plant chemicals for their “hormetic” effects. One



Mattson speaks with Dr. Paul Coates, director of NIH’s Office of Dietary Supplements, at the lecture.

Mattson

CONTINUED FROM PAGE 1

degeneration. Mattson’s research has shown that exercise and intermittent fasting can activate adaptive stress response pathways and may promote optimal function of cells.

“There’s evidence, mostly from animal models but also from an increasing number of epidemiological studies, to suggest that these changes that occur in the brain during aging, and are exacerbated in Alzheimer’s and Parkinson’s diseases, can be attenuated or counteracted by certain dietary and lifestyle [choices],” said Mattson.

In studies, sedentary mice exhibited much less brain activity than mice using a running wheel. Furthermore, when taught to touch icons on a computer screen for food rewards, Mattson said, the runner mice made fewer errors than did the sedentary ones, showing a correlation to the number of new neurons generated in the brain.

Mattson has observed healthy changes in people, too. While coaching his kids in cross-country, he said they concentrate better and are more cheerful during the running season. His lab studies routinely show that exercise improves cognitive function and can

Understanding the Metabolism of Bacteria Could Lead to Therapies

BY ERIC BOCK

Colonies of bacteria that attach to moist surfaces called biofilms can be found in many places—from the rust-colored sediment at the bottom of a lake to the lungs of a cystic fibrosis patient.

Learning how these bacterial colonies obtain the energy and nutrients they need to survive may one day lead to more effective treatments for bacterial infections, said Dr. Dianne Newman at a Wednesday Afternoon Lecture in Masur Auditorium on Jan. 13.

“Microbes have been dominating the biosphere for a large part of Earth’s history,” said Newman, professor of geobiology at California Institute of Technology’s division of geological and planetary sciences and division of biology. “For much of microbial history, the Earth did not have oxygen.”

Today, however, researchers often study microbes like bacteria only in oxygen-rich environments—overlooking their ability to switch easily to a no-oxygen setting. In her lab, Newman studies *Pseudomonas aeruginosa* PA14, a common bacterium that infects the lungs of patients with cystic fibrosis. She noted it takes about half an hour for *P. aeruginosa* to double in size in an oxygen-rich lab. If its growth were unchecked for a week, there would be enough bacteria to fill the volume of the known universe.

“Sustained fast growth rates are really lab artifacts and in the environment, obviously, this is not what’s going on,” Newman said.

Instead, something entirely different happens. Once biofilms reach a certain size, “the rate of oxygen consumption outpaces the rate of diffusion. Large portions of the biofilms are hypoxic or anoxic.” In other words, under low oxygen conditions, bacteria transition from an exponential growth phase to a stationary phase.

Take, for example, *Shewanella oneidensis* MR1, a bacterium first discovered at the bottom of Oneida Lake in New York. The organism forms biofilms on the surface of iron oxide minerals, which it utilizes to gain energy. When the biofilm

grows large enough, the bacteria in the middle don’t have access to oxygen or to the mineral. The middle bacteria, however, stay metabolically active. Early in her research, she suggested these bacteria produce extracellular organic molecules that allow electrons to move from the bacteria to the mineral.

A chemical process like this also happens in the lungs of patients with cystic fibrosis. Those with CF produce too much mucus in their lungs. The mucus blocks airways and makes it easy for bacteria to grow. Newman’s lab has a space in the CF pediatric clinic at Children’s Hospital Los Angeles in which they can analyze mucus as soon as it’s coughed up.

“Within these lungs, over time, a complex microbial community can accumulate and the

composition of this community can be very different from patient to patient. Yet, it’s fair to say that, among the pathogens that grow to be very successful in this habitat, is *P. aeruginosa*,” she said.

When *P. aeruginosa* cultures grow large enough, Newman explained, the bacteria produce phenazines—a type of molecule that is harmful to white blood cells called neutrophils and can

limit the growth of other bacterial strains in the presence of oxygen.

In the absence of oxygen, phenazines accept excess electrons within cells that can’t access oxygen or a mineral. This allows cells in the middle of the biofilm to remain viable. The phenazines transfer their electrons to something outside of the cell, such as oxygen or iron, allowing them to be recycled by the bacteria.

“As lung function declines, the concentration of phenazines rises very significantly,” she said. Before the decline, Newman has observed a higher concentration of a type of phenazine called pyocyanin.

Building upon her work with phenazines, Newman hopes to learn more about other aspects underpinning how *P. aeruginosa* survives under the slow-growth, anoxic conditions inside the lung mucus.

Insights into these processes may one day provide new avenues for treating the bacteria that colonize the lungs of people with cystic fibrosis, such as disrupting phenazine cycling in this environment.



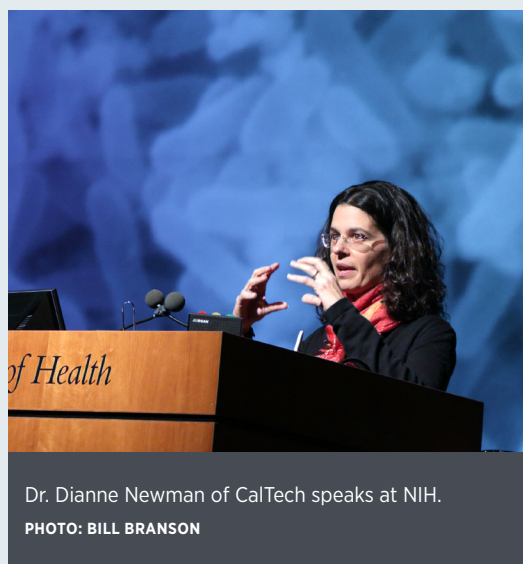
Mattson is known on campus as the coach/participant of an elite team that runs each year in the NIH Institute Relay.

such chemical, plumbagin, reduced brain damage in mice pretreated with it before they had a stroke. Other labs have found that quercetin, found in rhododendron and other plants and available in health food stores, protected cognitive function in Alzheimer’s and stroke models in mice and rats. Another compound, geraniin, also found in rhododendron, exhibited neuroprotective qualities and suppressed DNA damage relevant to Alzheimer’s, in certain doses. Other phytochemicals with restorative properties include galantamine, curcumin and capsaicin.

“From a lifelong health perspective, it’s important to challenge yourselves and your organ systems intermittently with things like exercise, not overeating, maybe even fasting a little bit. Maybe skip breakfast or lunch, then exercise, then eat,” said Mattson. “This is a mild stress on cells and cells respond adaptively by upregulating stress resistance pathways and autophagy [a sort of cellular garbage disposal system].”

But be sure to rest after vigorous exercise or moderate, intermittent fasting. “You don’t want to subject yourself to stress for an extended time period,” he said. Important processes take place during recovery, including protein synthesis and the formation of synapses. Mattson continues to test the theory that the cycles of challenge and recovery might promote optimal health.

So, the next time you’re out jogging or reducing your caloric intake or consuming a phytochemical, you just might be maintaining cellular health and starting a habit that may promote optimal brain health into a ripe, old age. **R**



Dr. Dianne Newman of CalTech speaks at NIH.

PHOTO: BILL BRANSON

Schizophrenia's Strongest Known Genetic Risk Deconstructed

Versions of a gene linked to schizophrenia may trigger runaway pruning of the teenage brain's still-maturing communications infrastructure, NIH-funded researchers have discovered. People with the illness show fewer such connections between neurons, or synapses. The gene switched on more in people with the suspect versions, who faced a higher risk of developing the disorder, characterized by hallucinations, delusions and impaired thinking and emotions.

"Normally, pruning gets rid of excess connections we no longer need, streamlining our brain for optimal performance, but too much pruning can impair mental function," said Dr. Thomas Lehner, director of the Office of Genomics Research Coordination at NIMH, which co-funded the study along with the Stanley Center for Psychiatric Research at the Broad Institute and other NIH components. "It could help explain schizophrenia's delayed age-of-onset of symptoms in late adolescence/early adulthood and shrinkage of the brain's working tissue. Interventions that put the brakes on this pruning process-gone-awry could prove transformative."

The gene, called C4 (complement component 4), sits in by far the tallest tower on schizophrenia's genomic "skyline" of more than 100 chromosomal sites harboring known genetic risk for the disorder. Affecting about 1 percent of the population, schizophrenia is known to be as much as 90 percent heritable, yet discovering how specific genes work to confer risk has proven elusive, until now.

A team of scientists led by Dr. Steve McCarroll of the Broad Institute and Harvard Medical School leveraged the statistical power conferred by analyzing the genomes of 65,000 people, 700 postmortem brains and the precision of mouse genetic engineering to discover the secrets of schizophrenia's strongest known genetic risk. C4's role represents the most compelling evidence, to date, linking specific gene versions to a biological process that could cause at least some cases of the illness. The results were published Jan. 27 in *Nature*.

"Since schizophrenia was first described over a century ago, its underlying biology has been a black box, in part because it has been virtually impossible to model the disorder in cells or animals," said McCarroll. "The human genome is providing a powerful new way [of prying] into this disease. Understanding these genetic effects on risk is a way of prying open that black box, peering inside and starting to see actual biological mechanisms."

More Than 1 in 20 U.S. Children Have Dizziness, Balance Problems

More than 1 in 20 (nearly 3.3 million) children between the ages of 3 and 17 have a dizziness or balance problem, according to an analysis of the first large-scale, nationally representative survey of these problems in U.S. children. Prevalence increases with age, with 7.5 percent of children ages 15-17 and 6 percent of children ages 12-14 having any dizziness or balance problem, compared with 3.6 percent of children ages 6-8 and 4.1 percent of children ages 3-5. The research was led by investigators at NIDCD.

Researchers found that girls have a higher prevalence of dizziness and balance problems compared to boys, 5.7 percent and 5 percent, respectively. In addition, non-Hispanic white children have an increased prevalence of dizziness and balance problems (6.1 percent) compared with Hispanic (4.6 percent) and non-Hispanic black (4.3 percent) children. The findings were published online Jan. 27 in the *Journal of Pediatrics*.

"These findings suggest that dizziness and balance problems are fairly common among children, and parents and providers should be aware of the impact these problems can have on our children," said Dr. James F.

Batthey, Jr., director of NIDCD and a pediatrician. "Parents who notice dizziness and balance problems in their children should consult a health care provider to rule out a serious underlying condition."

Previous estimates of dizziness and balance problems in children have ranged from 5 to 18 percent and have been based on limited, foreign, population-based studies.



Moderate hyperopia, if not treated, may affect reading ability and grade school readiness among preschoolers.

PHOTO: JOE BALINTFY

Uncorrected Farsightedness Linked to Literacy Deficits in Preschoolers

A study funded by NEI has shown that uncorrected farsightedness (hyperopia) in preschool children is associated with significantly worse performance on a test of early literacy.

The results of the Vision in Preschoolers-Hyperopia in Preschoolers study, which compared 4- and 5-year-old children with uncorrected hyperopia to children with normal vision, found that children with moderate hyperopia did significantly worse on the Test of Preschool Early Literacy than their normal-vision peers.

"This study suggests that an untreated vision problem in preschool, in this case one that makes it harder for children to see things up-close, can create literacy deficits that affect grade school readiness," said Dr. Maryann Redford, a program director in collaborative clinical research at NEI.

In most children with hyperopia, the condition is mild and has little impact on vision. A small number of preschool children have high hyperopia that is corrected with eyeglasses. It's estimated that 4-14 percent have moderate hyperopia, which often goes undiagnosed and untreated.

"Prior studies have linked uncorrected hyperopia and reading ability in school-age children," said Dr. Marjean Taylor Kulp, distinguished professor in the College of Optometry at Ohio State University and lead author of the study. "But large-scale investigations looking at reading readiness skills hadn't been conducted in preschool children. This study was necessary to determine whether or not, at this age, there was a link between the two."

The results were published Jan. 27 in *Ophthalmology*.

Zuk Named NIGMS Genetics Division Director

Dr. Dorit Zuk recently joined NIGMS as new director of its Division of Genetics and Developmental Biology (GDB). She is a molecular biologist whose research has focused on muscle development and RNA metabolism. She also has a strong background in science policy and communications.



Dr. Dorit Zuk

The GDB division funds basic research on the cellular and molecular mechanisms that underlie inheritance, gene expression and development, laying the foundation for advances in diagnosing, preventing, treating and curing a wide variety of diseases.

“GDB-funded researchers pursue questions about fundamental biological processes ranging from how cells repair DNA to how microbial diversity affects human health,” said NIGMS director Dr. Jon Lorsch. “Dr. Zuk’s expertise in genetics, developmental biology and other scientific fields, knowledge of many policy areas and ability to engage effectively with scientists and other stakeholders make her an ideal choice for this key position.”

Before coming to NIGMS, Zuk was director of the NCATS Office of Policy, Communications and Strategic Alliances. She previously served as science policy advisor to the NIH deputy director for extramural research. In this role, she developed, coordinated and disseminated policies and procedures on issues such as financial conflicts of interest and the future of the biomedical research workforce.

Zuk came to NIH in 2007 as an AAAS science and technology policy fellow. In 2008-2009, she served as a program officer for science policy and Hellman fellow at the American Academy of Arts and Sciences. She began her policy career after working in scientific publishing, serving as deputy editor of *Cell* from 2000 to 2002 and as editor of *Molecular Cell* from 2003 to 2007.

“I am excited to join NIGMS and the GDB division and look forward to working with the program staff and the extramural community to stimulate outstanding science that expands our knowledge of molecular mechanisms and developmental and cellular pathways,” said Zuk.

Zuk earned a B.Sc. in biology from Tel Aviv University and an M.Sc. in biology and a Ph.D. in cell biology from the Weizmann Institute of Science. She conducted postdoctoral research at the University of Massachusetts Medical School. Her honors include numerous NIH Director’s Awards, most recently for her work on an Ebola drug repurposing screening project.

New Members Appointed to NICHD Council

New appointments have been made to the National Advisory Child Health and Human Development Council, NICHD’s advisory body. Shown are (front, from l) Dr. Aaron Lopata, chief medical officer, maternal and child health, Health Resources and Services Administration; Dr. Constantine Stratakis, NICHD scientific



director; Dr. Catherine Spong, NICHD acting director; and Lesli Rotenburg, general manager, children’s programming, marketing and communications, PBS. In back are (from l) Dr. Timothy Shriver, chair and CEO, Special Olympics; Dr. Della Hann, NICHD associate director for extramural research; Dr. Atul Butte, director, Institute for Computational Health Sciences, University of California, San Francisco; Dr. DeWayne Pursley, associate professor of pediatrics, department of neonatology, Beth Israel Deaconess Medical Center/Harvard Medical School; and Dr. Richard Krugman, distinguished professor, pediatrics/child abuse, University of Colorado School of Medicine.

Liver Disease Patients Needed

An NIDDK research team seeks people with fatty liver disease to participate in a study. Researchers are looking at a breath test to measure how the body breaks down food in people with fatty liver disease. If you have been diagnosed with non-alcoholic fatty liver disease or steatohepatitis, you may be interested in participating. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 15-DK-0080.

Healthy Adults Sought

NHLBI researchers are studying the lungs of healthy adult volunteers to learn more about the causes and progression of lung diseases. At least one outpatient NIH visit is required. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 15-H-0017.

Volunteers Needed for Energy Study

NIDDK seeks healthy Caucasian men, 55-75 years old, and women 18-35 to participate in a research study. Doctors want to learn how the body burns energy at different temperatures. You will have an 8-day inpatient stay at the Clinical Center. Compensation is provided. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Refer to study 12-DK-0097.

Ketamine Study Recruiting Healthy Participants

An NIH research study is enrolling healthy persons ages 18 to 65 who are free of psychiatric disorders and certain medical conditions. Researchers will evaluate the effects of the experimental medication ketamine on brain receptors in healthy and depressed adults. Study includes 1 to 6 weeks of outpatient procedures: a screening visit, computer tasks, rating scales, neuropsychological testing, two intravenous infusions, a blood draw, brain scans (MEG & fMRI) and may include optional 2-4 overnight stays for a sleep study. The study is conducted at the Clinical Center. There is no cost to participate and compensation is provided. To find out if you qualify, email moodresearch@mail.nih.gov or call 1-877-MIND-NIH (1-877-646-3644), TTY 1-866-411-1010. Refer to study 04-M-0222.

'CUP' RUNNETH OVERTIME

Blizzard Calls Forth Best of NIH

Whether you called it Jonas, Snowzilla or something not suitable for an employee newsletter, the blizzard of Jan. 22-23 became an opportunity for NIH'ers to display their toughness and ingenuity.

The storm, which dumped about 2 feet of snow on the area, technically closed federal offices in the D.C. metro area for a few days, but that meant only that many employees teleworked from home, while others—those in charge of patient care, animal welfare, security and other critical services—showed up for work as usual and sometimes stayed way longer than expected.

On the telework side, according to the Center for Information Technology, normal VPN (virtual private network) usage averages about 2,500 connections per day. Those numbers spiked in the aftermath of the storm.

On Monday, Jan. 25, CIT had 9,996 unique VPN users. The next day, there were 10,383 unique VPN connections. "That was the peak," said Dan Luxenberg, senior advisor and acting service manager for communications and outreach at CIT.

While many NIH'ers can work remotely, the NIH security guard staff is expected to show up in inclement weather if at all possible. At the NIH Animal Center in Poolesville, one of the officers volunteered to pick up others in his all-terrain vehicle but was unable to give everyone a ride back home. That left some of the guards stranded at their duty station, with few roads in rural Poolesville cleared for safe travel. Some of the guards who made it in stayed for more than 2 days, with no facilities for sleeping and no snack shop or vending machines. The guards remained on hand to protect the facility, the workers deemed essential and the animals.

Said Dr. Charmaine Foltz, director, Division of Veterinary Resources: "For me, what is remarkable are the people who sleep at work to make sure that the animals are cared for. Contract staff stayed over Friday, Saturday and Sunday, both in Bethesda and Poolesville. Vets at both sites stayed over Friday and Saturday. Also,

remarkably, all vets were here Monday (Jan. 25) except one stuck in Atlanta."

According to the Office of Research Facilities' Division of Facilities Operations and Maintenance, on the Bethesda and Poolesville campuses:

■ Snow removal included 6 miles of roadway, 10 acres of parking lots and 21 miles of sidewalk. About 2.5 miles of road and 2 miles of sidewalk were kept open during the blizzard.

■ Equipment included more than 75 machines, ranging from large tractors with snow blowers and front-end loaders to sidewalk machines.

■ Labor time included 178 hours of 24/7 during the week of Jan. 22-29, with another 20 or so hours to go at press time.

■ More than 50,000 tons of snow were plowed and removed.

On campus, the NIH Central Utility Plant (CUP) staff "rose to the occasion in an exemplary way in preparation for the blizzard," said Brad Moss of ORS/ORF. "Pre-planning for the storm was critical. Twenty-seven staff remained in the CUP, around the clock, to ensure that CUP operations were maintained seamlessly."

The CUP is one of the largest utility plants in the U.S., producing steam, chilled water and cogenerated electrical and thermal energy for the Bethesda campus, Moss explained. Steam and chilled water is distributed via a complex network of more than 7 miles of pipeline.

The total energy production (electricity plus steam) from NIH's Central Utility Plant during the storm was equivalent to the hourly average consumption rate of approximately 63,000 households, said Moss.

At the Clinical Center, more than 250 staff slept over in order to be available for patient care. News media stories focused on nurse Alex Classen, who carried buckets of snow indoors so that an ill pediatric patient could enjoy it. Other patients, including some from Jamaica, had never seen snow and were glad to experience it.

On balance, though, most NIH'ers seemed glad to see the snowstorm go.



Few roads in rural Poolesville were cleared for safe travel, leaving some NIH security guards stranded at work.



Although stylishly accessorized with evergreen headress and oak-leaf scarf, Snowzilla nevertheless seemed to have endured much hardship, losing an eye at some point during the region's 4th biggest blizzard.



Front and back. Stalwart snow shovelers made every attempt to keep pace with the storm, constantly clearing the Clinical Center's entrances.